IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Stavrianopoulos et al.
Serial No.:	08/486,070
Filed:	June 7, 1995
For:	SOLID SUPPORT COMPRISING AN ARRAY OF SUBSTRATE SURFACES FOR NUCLEIC ACID ANALYSES AND APPLICATIONS, AND OTHER COMPOSITIONS AND SYSTEMS EMPLOYING CHEMICALLY LABELED OLIGONUCLEOTIDES OR POLYNUCLEOTIDES (As Previously Amended)

Group Art Unit: 1634

Examiner: Ardin H. Marschel, Ph.D.

P. O. Box 806
Pelham Manor, NY 10803

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

DECLARATION OF DR. CHERYL H. AGRIS, ATTORNEY AT LAW (IN SUPPORT OF THE WRITTEN DESCRIPTION OF THE INVENTION CLAIMED IN U.S. PATENT APPLICATION SERIAL NO. 08/486,070)

I, Cheryl H. Agris, hereby declare as follows:

1. I am a solo practitioner in patent law and intellectual property licensing matters, having been so engaged since 1998. Previous to that from 1992 to 1998, I was a patent attorney at Novo Nordisk of North America in New York City. Prior to my position at Novo Nordisk, I was a law clerk in the Biotechnology Group at the law firm of Pennie & Edmonds, also in New York City. I became a patent agent in 1990. As an attorney registered to practice before the U.S. Patent and Trademark Office, my present work involves the preparation and prosecution of U.S. patent applications in the biotechnology, pharmaceutical and chemical fields. I also oversee the foreign prosecution of patent applications. My present work also involves performing patentability and validity studies, infringement analysis and freedom of operation studies. As an intellectual property attorney, I have prepared licensing, consulting and confidentiality agreements for clients. I have also engaged in the peer review of patent prosecution by third parties. My legal and work experience at Novo Nordisk and Pennie & Edmonds is described in my Curriculum Vitae (CV) which is attached to my Declaration as Exhibit 1.

2. As described in the two paragraphs below, my scientific training and background predated my entry into the intellectual property field.

A. Before entering the intellectual property field, I was a scientist and researcher from 1979 - 1988. In 1979, I was an undergraduate research fellow at the Argonne National Laboratory in Argonne, Illinois. There, I analyzed bile acids isolated from the bile, urine, or serum from children with cholestatic liver disease using gas chromatography and gas chromatography/mass spectroscopy. Later from 1979 to 1986, I was a predoctoral fellow (graduate student) in the Division of Biophysics, Department of Biochemistry at the Johns Hopkins University (JHU) in Baltimore, Maryland. My thesis advisors were Dr. Paul O. P. Ts'o, Chair, Division of Biophysics and Dr. Paul S. Miller. While conducting my thesis research in Dr. Paul Miller's laboratory, I helped formulate methods for synthesizing nonionic oligonucleotide analogs and oligonucleoside methylphosphonates. As a member of Dr. Miller's group, I also studied the effects of oligonucleoside methylphosphonate sequences on the synthesis of VSV (vesicular stomatitis virus) proteins in cell culture and in vitro. In connection with my doctorate that I earned at JHU in 1986, I wrote a dissertation titled "Effects of Chemically Synthesized Oligodeoxyribonucleoside Methylphosphonates on Vesicular Stomatitis Virus Protein Synthesis and Infection." During my education and training at JHU, I co-authored a dozen papers with Dr. Miller, those papers being listed on my CV (Exhibit 1). While working in Dr. Miller's laboratory for several years, I became very familiar with the synthesis of oligonucleotides, particularly nonionic oligonucleotide analogs and oligonucleoside methylphosphonates, and the chemistry which we employed in Dr. Miller's laboratory to synthesize these compounds.

B. During the years 1986 - 1988, I was a research fellow at the Sloan Kettering Institute in New York City working in Dr. Robert Krug's laboratory. Dr. Krug was a member at that time of the Molecular Biology Program at Sloan Kettering where his research focused on transcriptional and translational control of influenza viral protein synthesis. While there, I investigated the mechanism of the block in the splicing of influenza viral NS1 mRNA to NS2 mRNA in vitro using molecular biological and biochemical approaches. During my graduate and post-

graduate years, I also became familiar with various formats used in nucleic acid detection and characterization, including solution hybridizations and mixed phase hybridizations, the latter involving immobilization of one of the nucleic acid reactants on a solid support, such as a nitrocellulose membrane. I am also familiar with two well-known scientific publications on membrane hybridizations, both of which were published in 1975: Southern, E.M. ["Detection of specific sequences among DNA fragments separated by gel electrophoresis," Journal of Molecular Biology 98:503-517 (1975)] and Grunstein and Hogness ["Colony Hybridization: A method for the isolation of cloned DNAs that contain a specific gene," Proc. Natl. Acad. Sci. (USA) 72:3961-3965 (1975)].

3. As indicated in my CV (Exhibit 1), my formal education includes three degr e programs. In 1979, I received my Bachelor of Arts in chemistry from Goucher College in Towson, Maryland. In 1986, I received my doctoral degree (Ph.D.) from the Johns Hopkins University, School of Hygiene and Public Health (Department of Biochemistry, Division of Biophysics). In 1992, I received my *Juris Doctor* degree from the Brooklyn Law School in Brooklyn, New York.

4. Among my publications are eight legal-related articles and fourteen scientific papers, including the dozen papers with Dr. Paul Miller referenced above in Paragraph 2. All of these publications are listed on pages 3-5 of my CV (Exhibit 1). Also listed are some representative U.S. patents among the approximately 150 U.S. patents in which I have participated in the preparation and/or prosecution. These representative U.S. patents are listed on page 5 of my CV (Exhibit 1).

5. Among my honors, awards and fellowships as listed on page 3 of my CV (Exhibit 1), I was a Richardson Scholar at Brooklyn Law School from 1988-1992. I was an American Cancer Society Fellow at the Sloan Kettering Institute between 1986-1988. In 1984, I received a Student Research Award from the Delta Omega Honorary Public Health Society. Between 1979 and 1986, I was the recipient of predoctoral training grants, first as an NIH predoctoral trainee (1979-1982) and later as a predoctoral trainee under the Albert Szent-Gyorgyi Foundation (1982-1986). When I graduated from college in May 1979, I received General Honors and Honors in Chemistry, in addition to having received the Louise Kelly Award in Chemistry. Previous to that, I worked in the Undergraduate Research Program

(January - May 1979) and in the Summer Graduate Student Program (June - August 1979) at Argonne National Laboratory.

6. My experience in continuing legal education has covered a number of significant areas in patent law. At various patent meetings and conferences, I have made several oral presentations on patent law, including, among others, issues related to the written description and enablement requirements under 35 U.S.C. §112, first paragraph. These presentations included the following: "Why Deposit Biological Materials?" New York, New Jersey, Connecticut, and Pennsylvania Joint Seminar on Developments in Patent Law, April 2000; "Inventorship" National Association of Patent Practitioners meeting, July 1999; "What to Claim in Biotechnology Patent Applications" National Association of Patent Practitioners meeting, October 1997; and "*In re Deuel*, Obviousness Standard for Biotechnology" BIO '96, June 1996.

7. Related to my efforts in the field of patent law are a number of faculty appointments and several oral presentations. These include: speaker on Intellectual Property Considerations in "Angel Financing: Navigating the Legal & Business Issues" at the Citybar Center for Continuing Legal Education (CLE), The Association of the Bar of the City of New York, November 28, 2000; organizer and instructor at the National Association of Patent Practitioner's 2000 Short Course on Nuts and Bolts of Patent Prosecution (July 2000); instructor at the Sixth, Eighth, Ninth and Tenth Annual Patent Prosecution Workshops: Advanced Claim Drafting and Amendment Writing (1996, 1998, 1999, 2000); and speaker at the Law Seminars: Biotechnology Key Legal & Business Issues, November 18-19, 1999 in Seattle, Washington. Each of these faculty appointments are listed on the third page of my CV (Exhibit 1). Among my oral presentations are two held last year and one each in 1999, 1998, 1997 and 1996. These presentations are also listed on pages 3-4 of my CV (Exhibit 1).

8. I have also attended the following continuing legal education programs in the intellectual property area. These include in the year 2000, Writing and Using Intellectual Property Opinions (Association of the Bar of the City of New York), and the International Intellectual Property Symposium at the Brooklyn Law School. In 1999, I attended the legal program Preparing Legal Opinions 1999: Intellectual

Property Due Diligence in Business Transactions, also with the Association of the Bar of the City of New York. In 1998, I took part in the New York, New Jersey, Connecticut and Pennsylvania Joint Seminar on Developments in Patent Law. In 1996, I attended "The Basics of Licensing and Licensing Law." I also attended two Patent Resources Group courses, "Advanced PCT Practice" and "European Patent Office Practice." In 1993, I attended the Practising Law Institute (PLI) program on Technology Licensing and Litigation. These are listed on the first page of my CV (Exhibit 1).

9. As a patent practitioner, I have lectured and written on the requirements of 35 U.S.C. §112, including the Written Description requirements under the first paragraph of §112, and I have also submitted comments on the Interim Written Description Guidelines issued July 7, 1998, 63 FR 32,639. I have read and reviewed the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, which were published on January 5, 2001 in the Federal Register, Vol. 66, No. 4, Pages 1099-1111. I am also familiar with the earlier Revised Interim Written Description Guidelines issued on December 21, 1999 as well as the Training Materials issued in conjunction with these Guidelines. My remarks below, opinions and conclusions with respect to the written description rejections are rendered in light of the aforementioned January 5, 2001 Guidelines. A copy of the January 5, 2001 Guidelines is attached to my Declaration as Exhibit 2.

10. I have been engaged by Enzo Biochem, Inc. as a scientific and legal consultant in order to review portions of the current prosecution of U.S. Patent Application Serial No. 08/486,070 (presently titled "Solid Support Comprising An Array of Substrate Surfaces For Nucleic Acid Analyses and Applications, And Other Compositions and Systems Employing Non-Radioactively Chemically Labeled Oligonucleotides or Polynucleotides") that was filed on June 7, 1995. I am being compensated by Enzo for this review and for making this Declaration. In connection with another of Enzo's pending patent applications, Serial No. 08/479,997, I also made a previous declaration for which I was compensated. Included for my present review were significant portions of the file wrapper for this

application, including: the original specification[1] (hereinafter "the '070 specification"), the previously pending claims in this application (183-318 and 325-717), an Office Action issued on September 7, 2000 including three cited references, Kourilsky et al., GB 2,019,408; Stuart et al., U.S. Patent No. 4,732,847; Ward et al., U.S. 4,711,955; and Applicants' March 7, 2001 Amendment Under 37 C.F.R. §1.115 (In Response To The September 7, 2000 Office Action) including new claims 718-1110 and five exhibits (Exhibits 1-5) submitted in that Amendment. A copy of claims 718-1110 is attached to my Declaration as Exhibit 3. I have also reviewed several other of Applicants' papers filed in connection with this application. These papers include Applicants' December 10, 1999 Fifth Supplemental Amendment, their November 1, 1999 Communication including Exhibits A-D, their August 20, 1999 Fourth Supplemental Amendment, their July 30, 1999 Communication including Exhibits A-D, and their May 18, 1999 Third Supplemental Amendment. I have also reviewed the Interview Summaries dated August 3, 1999, August 19, 1999, October 26, 1999, December 8, 1999, May 9, 2000 and December 5, 2000.

11. I generally agree with Applicants' remarks and positions as set forth in their responses referenced in the preceding paragraph, especially as such remarks and positions have applied to any claimed subject matter directed to arrays or solid supports comprising an array of substrate surfaces. In particular, I agree with the Applicants' remarks as set forth in their aforementioned March 7, 2001 Amendment Under 37 C.F.R. §1.115, beginning on page 54, last paragraph, and continuing through page 60, first full paragraph. A copy of those remarks is attached to my Declaration as Exhibit 4.

[1] I understand that the present application (Serial No. 08/486,070) is related to other prior applications in the family. The present application is a continuation of U.S. Patent Application Serial No. 07/967,646, filed on October 28, 1992, now abandoned, which in turn is a continuation of 07/607,347, filed on October 30, 1990, also abandoned, which is a continuation of U.S. Patent Application Serial No. 07/385,986, filed on July 20, 1989, the latter having issued as U.S. Patent No. 4,994,373 on February 19, 1991. The aforementioned Serial No. 07/385,986 is a continuation of U.S. Patent Application Serial No. 06/732,374, filed on May 9, 1985, also abandoned, and the last-mentioned Serial No. 06/732,374 is a continuation-in-part of U.S. Patent Application Serial No. 06/461,469, filed on January 21, 1983, also abandoned. The present specification is identical to the specification accorded Serial No. 06/732,374. I understand that a claim for priority has been made to both the first-filed application (Serial No. 06/461,469) and the second-filed application (Serial No. 06/732,374).

12. As I understand it, the claimed array invention as set forth in pending claim 718 (Exhibit 3) is directed to "[a] solid support comprising an array of substrate surfaces, each substrate surface comprising at least one double-stranded nucleic acid fixed or immobilized thereto, wherein at least one nucleic acid strand or a sequence therefrom comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable, and wherein at least one nucleic acid strand or a sequence therefrom in one of said substrate surfaces is different from at least one other nucleic acid strand or a sequence therefrom in another substrate surface." I understand that the claimed array invention as set forth in pending claim 800 is also directed to "[a] non-porous solid support comprising an array of substrate surfaces, each substrate surface comprising at least one nucleic acid strand fixed or immobilized thereto, and wherein at least one nucleic acid strand or a sequence therefrom in one of said substrate surfaces is different from at least one other nucleic acid strand or a sequence therefrom in another substrate surface." A number of dependent embodiments for the claimed array subject matter are recited in claims 719-799 and 801-872, which depend from claims 718 and 800, respectively.

13. I understand that in the latest September 7, 2000 Office Action, claims 325-376[2] were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention. On pages 4-5 of the Office Action, the Examiner stated:

> [1] In claims 325-376 arrays are claimed. These claimed arrays start with the broadest versions in claim 325 as only requiring a substrate surface with double-stranded nucleic acid fixed or immobilized thereto with at least one strand labeled as described in said claim. The closest array description, as filed, is given in the specification on page 16, lines 9-27. In this description the array also is limited to glass plates having depressions or wells with denatured analytes deposited therein, wherein single stranded analytes are fixed to the surfaces of the wells. Chemically labeled probes may then be hybridized to these analytes and subjected to detection of any probe-analyte hybrid. It is noted that the analytes are charact rized as being "various" which supports the presence of "different" analytes deposited in each well or depression. It is additionally noted that

[2] Former array claims 325-376 are the predecessor claims to pending array claims 718-872.

plastic wells are a disclosed option as given in the bridging sentence between pages 20 and 21 of the instant specification. Polystyrene microfilter wells are described on page 22, lines 10-12, as a solid support. The practice of fixing polynucleotide analytes to conventional microtiter plates is described on page 23 at the start of Example 7. In summary, the array embodiments, as filed, are all at least directed to solid supports with wells or depressions therein. It is lastly noted that instant claim 325 does not require either wells or depressions as being the form of the array of analyte fixation sites nor its being either glass or plastic, wherein microtiter arrays are deemed to be made of plastic. It is additionally noted that arrays of tubes or cuvettes as given in claim 340 has not been found as filed. Thus, the broader arrays as included in claim 325 contains NEW MATTER. Such broader array embodiments which are NEW MATTER, for example, include flat surface arrays or non-glass or non-plastic arrays. This NEW MATTER is contained in instant claims 325-376.

14. As Enzo's consultant and on its behalf, I am making this Declaration in support of the adequate written description of claims 718-872 (Exhibit 3) which were submitted with Applicants' March 7, 2001 Amendment Under 37 C.F.R. §1.115. As set forth in the paragraphs below, it is my opinion and conclusion that Applicants' claimed solid supports comprising an array of substrate surfaces, each substrate surface comprising at least one double-stranded nucleic acid fixed or immobilized thereto (in the case of claims 718-799) or at least one single stranded nucleic acid strand fixed or immobilized thereto (in the case of claims 800-872) are described in the '070 specification so as to reasonably convey to one skilled in the art that the Applicants had possession of such subject matter at the time their application was first filed. It is my further opinion and conclusion that depressions or wells are not essential or critical features of claims 718 and 800 taken as a whole, and that they need not be recited in either claim to meet the requirements for written description.

15. Based upon my own education, background, training and experience, I submit that at the time this application was first filed, a person of ordinary skill in the art relevant to the subject matter being claimed, including nucleic acid modification, synthesis, formatting, hybridization and detection, would have possessed or could have been actively pursuing an advanced degree in organic chemistry, the molecular biology field and/or biochemistry. Such an ordinarily skilled person could also be at least approaching or ranging toward the level of a junior faculty member with 2-5 years of relevant experience, or at least be a

postdoctoral student with several years of experience. I consider myself to possess the level of skill and knowledge of at least a person of ordinary skill in the art to which the present application and invention pertains.

16. I have reviewed the '070 specification as originally filed and as a skilled person in the art it is my opinion and conclusion that the original disclosure reasonably conveys that the Applicants were in possession of the subject matter of claims 718-872 when the application was first filed. Applicants' claimed subject matter meets the legal requirements for written description as the patent specification describes the claimed invention in "sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention" *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). Such possession may be shown by showing that the invention was "ready for patenting" such as by the disclosure of drawings or other descriptions of the invention that are sufficiently specific to enable a person skilled in the art to practice the invention. *Id.* When the elements recited in the claims are supported by corresponding language in the text, examples, drawings, or other disclosure in the specification, the written description requirement is satisfied and no further analysis is required. *In re Bowen*, 492 F.2d 859 (C.C.P.A. 1974). Furthermore, if new claims are proposed during prosecution, each claim must be expressly, implicitly or inherently supported in the originally filed disclosure and each claim must include all elements which applicant has described as essential. 66 FR at 1105. To establish inherency, it must be clear from any extrinsic evidence provided in the missing descriptive matter is necessarily present in the thing described in the reference and that it would be so recognized by persons of ordinary skill. *In re Robertson*, 169 F.3d 743, 49 USPQ2d 1949 (Fed. Cir. 1999).

APPLICANTS' DISCLOSURE DOES NOT LIMIT THEIR CLAIMED ARRAY INVENTION TO DEPRESSIONS OR WELLS.

17. Several portions in the '070 specification describe Applicants' claimed support comprising an array of substrate surfaces as set forth in claims 718-872 without limiting their invention to depressions or wells.[3] These several portions

[3] Numerous portions of the paragraphs below in my Declaration have been emphasized (in bold, italics or underline) in order to draw specific attention to such portions.

taken from the original specification and original claims are listed in the chart attached to my Declaration as Exhibit 5.

Example 1 (Pages 15-16)

A. The very portion of the '070 specification cited in the September 7, 2000 Office Action (page 16, lines 9-14) is part of the Detailed Description which deals with "methods for fixing the analyte to a **non-porous solid support**" (page 15, lines 9-10). Further, the portion cited in the Office Action is part of Example 1 which describes "an analyte [being] immobilized on a **solid support**, preferably a **non-porous translucent or transparent support** (page 15, lines 14-15). According to Example 1, "[t]o effect easy fixing of a denatured single-stranded DNA sequence to a **glass support**, one exemplary 'fixing' procedure may involve pretreating the glass by heating or boiling for a sufficient period of time in the presence of dilute aqueous nitric acid. Approximately forty-five minutes in 5% dilute acid should be adequate to leach boron residues from a borosilicate **glass surface**" (page 15, lines 16-23). In the next sentence, "[t]he **treated glass** is then washed or rinsed, preferably with distilled water, and dried at a temperature of about 115°C, for about 24 hours" (page 15, lines 23-25). "A 10 percent solution of gamma-aminopropyltriethoxysilane, which may be prepared by dissolving the above-identified silane in distilled water followed by addition of 6N hydrochloric acid to a pH of about 3.45, will then be applied to the **glass surface**" (page 15, lines 26-30). As described in Example 1, "the **glass surface** is then incubated in contact with the above-identified silane solution [10 percent solution of gamma-aminopropyltri-ethoxysilane] for about 2-3 hours at a temperature of about 45°C." (page 15, lines 31-33). Following that, "[t]he **glass surface** is then washed with an equal volume of water and dried overnight at a temperature of about 100°C. The resulting **treated glass surface** will now have available alkylamine thereon suitable for immobilizing or fixing any negatively charged polyelectrolytes applied thereto" (page 15, last four lines, through page 16, first three lines). In the next paragraph which contains the portion cited in the Office Action, "[s]uch treated glass could then be employed in the practice of the method of the invention. **For exampl , glass plates provided with an array of depr ssions or wells** would have samples of the various denatured analytes deposited therein, the single-stranded analytes being **fixed to the surfac s of th wells**. Thereupon, polynucleotide probes provided with

a chemical label may be deposited in each of the wells for hybridization to any complementary single-stranded analyte therein" (page 16, lines 8-17).

B. As a person of ordinary skill in the art, it is my opinion and conclusion that Example 1 in the '070 specification describes an array of substrate surfaces which are sub-elements of Applicants' claimed solid support. As quoted in the preceding paragraph above, an analyte is immobilized on a **solid support**, preferably a **non-porous translucent or transparent support** and a single-stranded DNA sequence is fixed to a **glass support**. To leach boron residues from a borosilicate **glass surface**, the glass is treated by heating or boiling in dilute aqueous nitric acid and then incubated in a silane solution to obtain a **treated glass surface** having available alkylamine thereon suitable for immobilizing or fixing any negatively charged polyelectrolytes applied thereto. The foregoing description reasonably conveys that single stranded nucleic acid [negatively charged polyelectrolytes] can be fixed or immobilized to the **treated glass surface** which has no limitation requiring depressions or wells. Such negatively charged electrolytes, i.e., nucleic acids, which are fixed or immobilized to a **treated glass surface** also defines an array as set forth in Applicants' claimed invention.

C. Even when the '070 specification describes an array having depressions or wells (page 16, lines 10-11), that description does not characterize such depressions or wells as being a critical or essential feature of Applicants' claimed array invention. Instead, the depressions or wells in the glass plates are offered only as an "example" and illustration. It is significant that the very sentence in question (page 16, lines 10-11) begins with the introductory phrase "[f]or example." Thus, it is my opinion and conclusion that depressions or wells are but one example of Applicants' claimed solid support and not a limitation *per se* on their claimed array invention. Taking both paragraphs in Example 1 together, the '070 specification reasonably conveys to a person skilled in the art that nucleic acids can be fixed or immobilized in the form of an array to **non-porous solid supports**, such as **glass supports, glass surfaces** and **treated glass surfaces**. The descriptions in Example 1 are sufficiently specific to enable a person skilled in the art to practice the invention which demonstrates that Applicanats' claimed array invention was "ready for patenting." Therefore, Example 1 shows Applicants' clear possession of their claimed array subject matter.

Other Examples (2-7) in the Detailed Description (Pages 16-25)

18. As explained in Paragraph 16A above, the Detailed Description in the '070 specification begins on page 15 (lines 5-11) and precedes Example 1 and the rest of Examples 2-7. The Detailed Description recites:

> The following examples are illustrative of preferred embodiments of the method of the present invention. Specifically referred to therein are methods for fixing the analyte to a **non-porous solid support**, as well as illustrations of the use of soluble signals in polynucleotide probes as discussed above.

As explained in Applicants' March 7, 2001 Amendment, different forms of the non-porous solid support recited above are disclosed in the rest of Examples 2-7:

Example 2: the **glass surface treated** as described in Example 1

Example 3: **activated glass surface (glass tubes)**

Example 5: **non-porous plastic surface**
polystyrene
DDA added to polystyrene
polylysine (PPL) treated plastic surface
plastic surface
polystyrene plates

Example 6: **polystyrene plates**
polystyrene microfilter wells
6-aminohexane linked polystyrene
non-porous siliceous solid support such as **glass** and **plastic**
non-porous siliceous solid support (glass and plastic) treated with coating of epoxy resin (epoxy glues)

Example 7: **conventional microtiter well plates**
conventional microtiter well plates treated with ammonium acetate

It is my opinion and conclusion that in reading the Detailed Description and Examples 1-7 in the '070 specification, a skilled person would understand that Applicants' claimed solid support comprising an array of substrate surfaces would

include a number of materials, such as glass, plastic, treated glass and treated plastic, and that such materials are not limited to "depressions or wells."

Devices and Conventional Laboratory Apparatus

19. It is my further opinion and conclusion that other portions in the '070 specification relating to devices and apparatuses describe Applicants' claimed solid support comprising an array of substrate surfaces.

A. As explained in Applicants' March 7, 2001 Amendment, the '070 specification expressly *equates* "device" with "solid support" in the first paragraph on page 14:

> . . . ***It may also be desirable for*** both the solid support to which the analyte is fixed and the device to be composed of the same material, or for ***the device to function as the support*** in addition to facilitating spectrophotometric detection.

B. "Devices" are also described in the second paragraph on page 14:

> . . . A related product of the invention is an apparatus comprising a **plurality of such devices** for containing a fluid, **in which at least one such device contains the above-described immobilized polynucleotide sequence**, polynucleotide or oligonucleotide probe, signalling moiety, and soluble signal.

C. Previously, beginning with the last four lines on page 13, and continuing through the first line on page 14 in the specification, devices are further described in the '070 specification:

> . . . ***Examples of devices*** useful in the spectrophotometric analysis of the signal include ***conventional apparatus*** employed in diagnostic laboratories, i.e., plastic or glass wells, tubes, cuvettes or arrangements of wells, tubes or cuvettes.

D. Continuing on page 14, lines 19-20 in the '070 specification, devices are further described:

> . . . The ***portion of the device for containing the fluid*** is desirably a ***well, a tube, or a cuvette***.

E. The above-quoted portions directed to devices and conventional laboratory apparatus reasonably convey to the skilled person that Applicants' claimed solid support comprising an array of substrate surfaces can usefully take the form of such devices and conventional laboratory apparatus which are not limited to "depressions or wells."

Originally Filed Claims

20. The originally filed claims in Applicants' disclosure also support the description of their claimed array invention.

A. "Device" is defined in originally filed claim 17 from the specification:

> Claim 17. The method in accordance with Claim 16, characterized in that said ***device*** is selected from the group consisting of ***a well, a tube, a cuvette and an apparatus which comprises a plurality of said wells, tubes or cuvettes***.

B. The "means for containing a fluid" recited in original claim 17 is also defined by originally filed claim 23[4]:

> Claim 23 An **apparatus** comprising:
> a **plurality of means for containing a fluid**[5], wherein at least one of said means comprises:
> (i) an ***immobilized polynucleotide sequence hybridized to a polynucleotide or oligonucleotide probe***, said probe having covalently attached thereto a chemical label comprising a signalling moiety capable of forming a soluble signal, and
> (ii) a soluble signal generated by means of said signalling moiety.

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[4] The means for containing a fluid language in claim 23 is also found in originally filed claim 21 from the specification:

> Claim 21. The *device* according to Claim 20, wherein said *means for containing a fluid* is selected from the group consisting of *a well, a tube, and a cuvette*.

[5] The above-recited means for containing a fluid is also found in originally filed claim 21 from the specification:

> Claim 21. The *device* according to Claim 20, wherein said *means for containing a fluid* is selected from the group consisting of *a well, a tube, and a cuvette*.

C. It should not in any way be overlooked that through the phenomenon of surface tension, fluids can be contained on a surface, even a flat or planar surface, such as a glass slide. As is often described in elementary physics textbooks, the cohesive forces resulting from attraction between like particles in a fluid, such as water molecules in water, act to pull the surface particles inward and away from the surface. The result is surface tension which pulls drops and bubbles into spheres on a surface. The curved surface of a water drop on a surface is flattened slightly by gravity. This is illustrated in The Visual Dictionary of Physics, Jack Challoner, DK Publishing, Inc., New York, NY, 1995, page 26, in the upper right corner (copy attached as Exhibit 6). Surface tension has been used in microarray technology by at least one microchip manufacturer to attach nucleic acids to the solid surface of a glass slide to form a microarray of oligonucleotides. Using differences in surface tension imparted by chemical coatings, reagents containing nucleic acids are localized to very specific areas on the microarray. See the attached three pages from Protogene, Inc. of Menlo Park, California, copy attached as Exhibit 7.

21. I also agree with Applicants' remarks in their March 7, 2001 Amendment that in a great number of instances their disclosure refers to fixation or immobilization of nucleic acid to "surfaces." As explained by Applicants in their Amendment, it is ultimately the ***surface of a solid support*** (device or conventional laboratory apparatus, means for containing a fluid, well or depression, tube or cuvette) to which nucleic acid is being fixed or immobilized. Again, in several instances, the '070 specification refers to the surface as the point of fixation or immobilization:

a) Example 2

"A ***glass surface*** as described in Example 1 can be employed . . .

b) Example 3

. . . In these tests, the analyte, phage lambda DNA, was immobilized on an activated ***glass surface*** . . .

c) Example 5

The advantages of the practices of this invention are also obtainable when the probe is immobilized on a ***non-porous plastic surface***. When a ***plastic surface*** is

employed, it is sometimes desirable to increase the effectiveness or uniformity of the fixation by pretreating the ***plastic surface***.

Because polystyrene from various batches or sources exhibits different binding capacities, the adherence or fixing of DNA to a ***polystyrene surface*** is improved by ***treating the surface*** with an amino-substituted hydrophobic polymer or material. . . Another technique for improving the fixing or uniformity of the ***plastic surface*** for fixing DNA involves ***treatment of the surface*** with polylysine (PL).

In tests involving the fixing the DNA to a ***plastic surface***, biotinylated DNA (bDNA) was denatured and aliquoted into Dynatech, Immulon II™ removeable wells.

d) Example 6

An improved capability for fixing or immobilization of DNA to non-porous siliceous solid supports, such as glass and plastic, is also provided by treatment with a coating of an epoxy resin. For example, ***treatment of glass or polystyrene surfaces*** with commercially available epoxy glues, such as a solution of epoxy glue in ethanol [1 percent w/v] serves this purpose. These epoxy solutions are applied to the ***surfaces or wells***, and the solvent, ethanol, evaporated thereon at a temperature of 37 C, thereby providing a polyamine polymeric coating on the ***treated surface***. These ***surfaces*** were found to absorb ^{3}H-labeled DNA from aqueous solution at pH less than 9.5.

It is my opinion and conclusion that a skilled person reading the '070 specification, and the above-quoted portions specifically, would understand that Applicants' disclosure covering their claimed array invention extends far beyond the passage quoted in the Office Action (page 16, lines 9-27 in the '070 specification). Such a skilled person would understand that Applicants' claimed invention can take the form of a number of different solid supports and devices, that the solid supports and devices described in the '070 specification can be functionally the equivalent of each other, and that the surface of any solid support or device (or conventional laboratory apparatus) can be treated in accordance with Applicants' disclosure to effect fixation or immobilization of nucleic acid thereto.

APPLICANTS HAVE DISCLOSED A REPRESENTATIVE NUMBER OF SPECIES TO SUPPORT THE GENERIC SUBJECT MATTER OF CLAIMS 718 AND 800.

22. According to the January 5, 2001 Written Description Guidelines, "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. The latter is defined in the January 5, 2001 Guidelines thusly:

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus. [66 FR at 1106]

A. In Applicants' March 7, 2001 Amendment, two charts were submitted as Exhibits 2 and 3 to that paper. Both charts depicted the nature of Applicants' claimed solid support and its relationship to other elements or sub-elements disclosed in the '070 specification, including the instantly claimed array of substrate surfaces. Both charts are also attached to my Declaration as Exhibits 8 and 9.[6] As shown in the two charts (Exhibits 8 and 9), the solid support can be porous and non-porous, and transparent or translucent in the case of either. Polymeric materials can be used to construct the porous solid support or the non-porous solid support. In the case of the porous solid supports, such polymeric materials include porous glass, nitrocellulose filters, dextran and treated porous glass. In the case of non-porous solid supports, polymeric materials include dextran, plastic and glass. Plastics can include polystyrene, polyethylene and polypropylene. Treated surfaces include treated plastic and treated glass. The former includes treatment with duodecadiamine (DDA), polylysine (PPL), epoxy resin or glues, ammonium acetate (NH_4OAc) and amino-derivitized. The latter, treated glass, includes treatment with γ-aminopropyltriethoxysilane, coating solution, epoxy resin or glues and ammonium acetate (NH_4OAc).

[6] As indicated in the charts (Exhibits 8 and 9), Applicants' claimed arrays were recognized in the September 7, 2000 Office Action to cover both glass and plastic and depressions and wells, shown in green in both charts. To the extent that they include flat surface arrays or non-glass or non-plastic arrays, Applicants' claimed arrays were rejected for new matter.

B. As also noted in Applicants' March 7, 2001 Amendment, the specification quite clearly and significantly equates "device" with "solid support" in the first paragraph on page 14:

> . . . ***It may also be desirable for*** both the solid support to which the analyte is fixed and the device to be composed of the same material, or for ***the device to function as the support*** in addition to facilitating spectrophotometric detection. [emphasis added]

The device can include an apparatus, a portion for retaining a fluid, light transmitting capabilities and means for containing a fluid. The apparatus can take the form of a plurality of means for containing a fluid and a plurality of devices for containing a fluid. The latter can take the form of wells, tubes and cuvettes, as can the portion of the device for retaining a fluid. The light transmitting device can assume a number of embodiments, including conventional laboratory apparatus, plastic wells, glass wells, tubes, cuvettes, and an arrangement of wells, tubes or cuvettes. The means for containing a fluid in a device can be a well, a tube or a cuvette.

C. I would also like to point out that

First, the Examiner has recognized claim coverage for

GLASS OR PLASTIC ARRAYS HAVING DEPRESSIONS OR WELLS.

Second, the original specification describes an

APPARATUS COMPRISING A PLURALITY OF DEVICES FOR CONTAINING A FLUID, IN WHICH AT LEAST ONE SUCH DEVICE CONTAINS THE ABOVE-DESCRIBED IMMOBILIZED POLYNUCLEOTIDE SEQUENCE, POLYNUCLEOTIDE OR OLIGONUCLEOTIDE PROBE, . . .

Third, the specification describes the device as

CONVENTIONAL APPARATUS EMPLOYED IN DIAGNOSTIC LABORATORIES, I.E., PLASTIC OR GLASS WELLS, TUBES, CUVETTES OR ARRANGEMENTS OF WELLS, TUBES OR CUVETTES.

Fourth, the specification also describes

THE PORTION OF THE DEVICE FOR CONTAINING THE FLUID IS DESIRABLY A WELL, A TUBE, OR A CUVETTE.

Fifth, original claim 23 defines

AN APPARATUS COMPRISING A PLURALITY OF MEANS FOR CONTAINING A FLUID, WHEREIN AT LEAST ONE OF SAID MEANS COMPRISES: (i) AN IMMOBILIZED POLYNUCLEOTIDE SEQUENCE HYBRIDIZED TO A POLYNUCLEOTIDE OR OLIGONUCLEOTIDE PROBE, . . .

Sixth, means for containing a fluid are defined in original claim 21 as being

SELECTED FROM THE GROUP CONSISTING OF A WELL, A TUBE, AND A CUVETTE.

Fixation or immobilization of nucleic acids occurs through the surfaces of the solid support which are described numerously in the specification as follows:

EXAMPLE 2 ("GLASS SURFACE")
EXAMPLE 3 ("GLASS SURFACE")
EXAMPLE 5 ("PLASTIC SURFACE" OR "NON-POROUS PLASTIC SURFACE")
EXAMPLE 6 ("GLASS OR POLYSTYRENE SURFACES").

D. Example 6 also discloses that epoxy solutions are applied to the

SURFACES OR WELLS.

Specifically, Example 6 states:

> For example, ***treatment of glass or polystyrene surfaces*** with commercially available epoxy glues, such as a solution of epoxy glue in ethanol [1 percent w/v] serves this purpose. ***These epoxy solution are applied to the surfaces or wells***, and the solvent, ethanol, evaporated thereupon at a temperature of 37°C, thereby providing a polyamine polymeric coating on the treated surface.

E. It is my opinion and conclusion that the specification and original claims disclose the following embodiments:

GLASS OR PLASTIC ARRAYS HAVING WELLS OR DEPRESSIONS OR OTHERE SURFACES OR BEING A PLURALITY OF DEVICES OR MEANS FOR CONTAINING A FLUID WHICH ARE DESIRABLY WELLS, TUBES OR CUVETTES OR AN ARRANGEMENT OF WELLS,TUBES OR CUVETTES.

F. It is my opinion and conclusion that a representative number of species are described in the '070 specification to support the breadth of Applicants' claimed array invention. One of ordinary skill in the art would recognize that Applicants were in possession of the necessary common attributes or feature of the elements possessed by the members of the genus in view of the great number of species disclosed, specifically, "a solid support comprising an array of substrate surfaces". As discussed in several paragraphs above, arrays are described in Example 1 not only as an example for "depressions or wells," but also for solid supports in general, and glass supports and treated glass surfaces in particular. Devices, containing means, apparatus, conventional laboratory apparatus, tubes and cuvettes are also representative species which are disclosed in the '070 specification.

APPLICANTS' CLAIMED ARRAY INVENTION DOES NOT OMIT AN ESSENTIAL ELEMENT.

23. I have read and agree with Applicants' remarks regarding the omitted essential element rule as set forth in their March 7, 2001 Amendment beginning on page 58, second full paragraph, and continuing through page 60, first paragraph (Exhibit 4). In addition to the *Gentry* and *Reiffin* cases, [*Gentry Gallery, Inc. v. Berkline Corporation*, 134 F.3d 1473 (Fed. Cir. 1998), 45 USPQ2d 1498 (Fed. Cir. 1998) and *Reiffin v. Microsoft Corp.*, 48 USPQ2d 1274 (N.D. Calif. 1998)], another case related to this doctrine is *In re Peters*, 221 USPQ 952 (CCPA 1983). In the Peters case, a reissue application had been filed where the independent claim was broadened to so that it covered tapered and nontapered tips. The original claims had recited that the tips were tapered. The specification disclosed that the tip had a thickness at its base substantially equal to that of the support wall and tapering toward the front wall. The claims were rejected on the grounds that there was a lack of support in the original disclosure for the nontapered tips. The Board upheld the rejection indicating that the disclosed tip configuration was critical to the invention. The CCPA reversed the Board's decision stating:

> No prior art was distinguished from and no rejection was overcome on the basis of the tip shape. Most importantly, one skilled in the art would readily understand that in practicing the invention it is unimportant whether the tips are tapered, and the board erred in determining the contrary.
>
> The broadened claims merely omit an unnecessary limitation that had restricted one element of the invention to the exact and noncritical shape disclosed in the original patent. In sum, nothing in the original disclosure indicates or suggests that the tapered shape of the tips was essential or critical to either the operation or patentability of the invention. [*Id* at 953.]

The precise form of Applicants' claimed array is not described in the '070 specification to be essential or critical to the practice of their invention. As described earlier in paragraphs 17-22 above, the array of substrate surfaces can take any number of forms, including depressions, wells, tubes, cuvettes, solid supports, non-porous solid supports, glass supports, treated glass surfaces, plastic surfaces, treated plastic surfaces, devices, conventional laboratory apparatus, and so on. Armed with the '070 specification, a person of ordinary skill in the art would recognize the non-essential or non-critical nature of depressions or wells with respect to Applicants' claimed array invention. This is particularly so since no statement or reference appears in the '070 specification which identifies depressions or wells as being essential or critical features.

24. I wish to point out that Applicants' disclosure and their claimed subject matter also meets the January 5, 2001 Written Description Guidelines (Exhibit 2), particularly with respect to the their claimed solid support comprising an array of substrate surfaces.

A. Those guidelines provide that the written description requirement is met when the patent specification describes the claimed invention in "sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention" (citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991) 66 FR 1099 (2001). According to these guidelines, possession may be shown by showing that the invention was "ready for patenting" such as by the disclosure of drawings or oth r descriptions of the invention that are sufficiently specific to enable a person skilled in the art to

practice the invention. *Id.* It is well established case law that when the elements recited in the claims are supported by corresponding language in the text, examples, drawings, or other disclosure in the specification, the written description requirement is satisfied and no further analysis is required. *In re Bowen*, 492 F.2d 859 (C.C.P.A. 1974). Furthermore, if new claims are proposed during prosecution, each claim must be expressly, implicitly or inherently supported in the originally filed disclosure and each claim must include all elements which applicant has described as essential. 66 FR at 1105. To establish inherency, it must be clear from any extrinsic evidence provided in the missing descriptive matter is necessarily present in the thing described in the reference and that it would be so recognized by persons of ordinary skill. *In re Robertson*, 169 F.3d 743, 49 USPQ2d 1949 (Fed. Cir. 1999).

B. The Written Description Guidelines state the following with respect to "New matter:"

> The proscription against the introduction of new matter in a patent application (citation omitted) serves to prevent an applicant from adding information that goes beyond the subject matter originally filed (citation omitted). Thus, the written description requirement prevents an applicant from claiming subject matter that was not adequately described in the specification as filed. New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement (citation omitted). While there is not *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit or inherent disclosure.

Given the numerous embodiments for Applicants' claimed array invention as set forth in Paragraphs 17-22 above, it is my opinion and conclusion that the original disclosure supports the subject matter of claims 718 and 800, and, therefore, meets the January 5, 2001 Written Description Guidelines.

C. One particular case is on point with respect to new matter and that case is *In re Rasmussen*, 211 USPQ 323 (CCPA 1981). In *Rasmussen*, th claim at issue was amended to recite the adhering step as "adheringly applying" one layer of tube to an adjacent earlier layer for language in the original claim specifying the use of adhesives. The specification described the step as follows:

> [A]dhesive is applied to the tubular foil 4 in a narrow or broader strip, possibly in two narrow strips. Accordingly, the face of the tubular foil successively sticks to the winding lying on the drums.
>
> *Id.* at 326.

A new matter rejection had been made on the grounds that limiting the scope of the original disclosure to the use of adhesives would have meant that allowance of the broader claim would be an enlargement of the scope of the disclosure. The Board affirmed reasoning that the application only disclosed one embodiment and that broadening the scope of the claim added new matter to the application. *Id.* at 325. The CCPA reversed the Board's decision. The Court noted that broadening a claim does not add new matter to the disclosure and that an applicant is entitled to claims as broad as the prior art and the disclosure will allow. Most importantly, the Court noted that :

> . . . one skilled in the art who read Rasmussen's specification would understand that it is unimportant *how* the layers are adhered, so long as they are adhered. Thus the phrase"adheringly applying" is supported by the example found in the specification.
>
> *Id.* at 327.

In the case of claims 718 and 800, one of ordinary skill in the art would certainly have understood from reading the '070 specification that the precise form of the solid support or the array of substrate surfaces is unimportant, and that depressions or wells are not necessary in order to practice Applicants' claimed array invention.

D. Another case on point with new matter is *Kolmes v. World Fibers Corporation*, 107 F.3d 1534, 41 USPQ2d 1829 (Fed. Cir. 1997). In *Kolmes*, a new claim to a non-metallic cut resistant yarn recited two strands, where the two strands are wrapped about a non-metallic core at the rate of 8-12 turns per inch. Finding that this claim did not contain new matter, the Court held:

> At col. 5, lines 38-40, the specification states that the coverings or wrappings are formed "at the rate of 4-12 turns per inch, with 8 turns per inch being preferred." All the claimed limitations including the 8-12 turns per inch are thus well supported by the specification. Although the text of the specification only discusses the clamed wrapping rate with reference to a figure showing a one strand core, the specification discloses a two strand core with a two strand

> covering. World has not shown that the specification as a whole would have failed to convey to one skilled in the art the use of the claimed wrapping rate with a two strand core (citations omitted). Claims to subject matter disclosed in the specification are not new matter.

In the case of the present application, the term "array" is specifically stated on page 16 (lines 10-11) and an "array of depressions or wells" is described on the same page at lines 9-27. Numerous other materials that can be used in Applicants' claimed array invention are disclosed in the specification. Examples 2-7 disclose a number of different forms of the non-porous solid support. On page 14 (lines 1-6), the '070 specification equates "device" with "solid support." Thus, an array can be accurately characterized as a device or a plurality of devices or means for retaining or containing a fluid.

APPLICANTS' CLAIMED ARRAY INVENTION ALSO MEETS THE TEST FOR WRITTEN DESCRIPTION PROVIDED IN THE DECISION TREE TRAINING MATERIALS.

25. I would also point out that training materials have also been provided in connection with the Revised Interim Written Description Guidelines issued on December 21, 1999. A decision tree was included with those training materials and is attached to my Declaration as Exhibit 10. Although revisions are expected to the training materials in view of the final Written Description Guidelines, these training materials appear to be still in effect. 66 FR at 1099. When a claim of broader scope is added, the question posed is "Is an element(s) missing from the claim?" If the answer is "yes", the question posed is "Is the missing element(s) described by applicant as being an essential or critical feature of the new claim as a whole?" If the answer is "no", the question posed is "Is there express, inherent or implicit support for the claim as a whole?" If the answer is "yes", the written description requirement is met.

26. Under the decision tree analysis described in the preceding paragraph (25), it is my opinion and conclusion that Applicants' claimed array invention meets the written description requirements of 35 U.S.C. §112, first paragraph. If one accepts that depressions or wells are missing as elements from claims 718 and 800, the next step in the decision tree analysis calls for asking whether

depressions or wells have been described by Applicants in the '070 specification as being essential or critical features of new claims 718 and 800 as a whole. Having read the '070 specification, it is my opinion and conclusion as a person of ordinary skill in the art that Applicants have only described depressions or wells as embodiments for the newly claimed solid support, which is evidenced by the use of the introductory "[f]or example" phrase on page 16, lines 9-10). Depressions or wells are nowhere in the '070 specification described as essential or critical features of Applicants' claimed invention. Therefore, the written description requirement has been met.

THERE ARE NO OTHER LEGAL BASES FOR COMPELLING APPLICANTS TO LIMIT THEIR CLAIMED ARRAY INVENTION TO DEPRESSIONS OR WELLS.

27. Before closing, I would like to point out that there is no *ipsis verbis* requirement under the law for written description. It is not necessary that there be literal support for the change in the language desired. The description need not be in *ipsis verbis* to be sufficient. *Martin v. Johnson,* 172 USPQ 391, 395 (CCPA 1972). It is sufficient that the specification "convey clearly to those skilled in the art, to whom it is addressed, in any way, the information that the applicant has invented the specific subject matter later claimed." *In re Wertheim,* 191 USPQ 90, 97 (CCPA 1973). With respect to new matter in the claims, the Written Description Guidelines state:

> New claims, amended claims or claims asserting entitlement to the benefit of an earlier priority date or filing date under 35 U.S.C. 119, 120 or 365(c)....To comply with the written description requirement of 35 U.S.C. 112, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120 or 365(c), each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure. 66 FR 1099, 1106-1107

Additionally, as stated in *Reiffin v. Microsoft Corp.* 48 USPQ2d 1274, 1276 (Fed. Cir. 1998), cited *supra*.:

> . . . it is fairly well established that a patent owner may assert claims which go beyond the specific embodiment shown in his application. See *Ethicon Endo-Surgery, Inc. v. United States Surgical Corp.,* 93F.3d 1572, 1582 n. 7 [40 USPQ2d 1019] (Fed. Cir. 1996). The classic example of the *Ethicon* principle involves a patent on a barn.

> Even if the patent owner's application contained a preferred embodiment that depicted only a red barn, the patent owner would not necessarily be foreclosed from asserting a claim over a brown barn.

In *Ethicon*, the Court had held that a claim added in a reissue application directed to a surgical stapler where the exact location of a lockout mechanism is not specified was nevertheless supported by the specification even though the specification had specified only one location. The Court's reasoning ran as follows. If the applicant did not consider the precise location of the lockout to be an element of the invention, the applicant was free to draft the claim broadly within the limits imposed by the prior art to exclude the lockout's exact location as a limitation of the claimed invention. Similarly, in the '070 specification, I can find no disclosure which would limit Applicants' claimed array invention to depressions or wells. As indicated above (paragraphs 17C and 26), the passage cited in the Office Action (page 16, lines 9-27) begins with the introductory phase "***For example,*** . . ." Moreover, no prior art rejections have been raised in this application which would have necessitated a discussion of specific array types. Therefore, under the January 5, 2001 Written Description Guidelines and the *Ethicon* holding, Applicants should not be required in this instance to limit their claimed array invention to depressions or wells.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of the application or any patent issued thereon.

5/8/01
Date

Cheryl H. Agris
Cheryl H. Agris, Ph.D.
Attorney At Law

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FinalDeclaration.CHA.5.7.01

CHERYL HEATHER AGRIS

P.O. Box 806
Pelham, New York 10803
(914) 712-0093 (telephone)
(914) 712-0094/5 (telefax)
c.agris.patlaw@pobox.com

DEGREE PROGRAMS:

1992: J.D., Brooklyn Law School
Top 15%

1986: Ph.D., The Johns Hopkins University, Baltimore, Maryland
School of Hygiene and Public Health
Department of Biochemistry, Division of Biophysics
Thesis: "Effects of Oligonucleoside Methylphosphonates on Vesicular Stomatitis Virus Protein Synthesis and Infection"

1979: Bachelor of Arts, Chemistry, Goucher College,
Towson, Maryland
Cumulative grade point average: 3.57/4.00

CONTINUING EDUCATION:

2000: NASD Arbitrator Training Program; Writing and Using Intellectual Property Opinions (Association of the Bar of the City of New York); International Intellectual Property Symposium, Brooklyn Law School; Preparing Legal Opinions 1999: Intellectual Property Due Diligence in Business Transactions (Association of the Bar of the City of New York)

1998: New York, New Jersey, Connecticut, and Pennsylvania Joint Seminar on Developments in Patent Law

1996: The Basics of Licensing and Licensing Law (The Licensing Journal)

1995: Patent Aspects of GATT (ABA, Section of Intellectual Property Law)
Advanced PCT Practice (Patent Resources Group)

1994: European Patent Office Practice (Patent Resources Group)

1993: Technology Licensing and Litigation (Practicing Law Institute)

ADMISSIONS:

New York and New Jersey State Bars
Registered to practice before the U.S. Patent and Trademark Office

LEGAL EXPERIENCE:

1998 - present: Solo practitioner
Preparation and prosecution of U.S. patent applications in the biotechnology, pharmaceutical and chemical fields; overseeing foreign prosecution of patent applications; patentability and validity studies; infringement analysis; freedom of operation studies; preparation of licensing, consulting and confidentiality agreements; peer review of patent prosecution by third parties; arbitrator

1992 - 1998: Patent Attorney, Novo Nordisk of North America, N.Y., N.Y.
Preparation and prosecution of U.S. patent applications in the biotechnology and chemical fields; prosecution of foreign applications in the United States in the biotechnology, chemical, and pharmaceutical fields; supervising foreign filings; supervising patent liaison in California subsidiary; patentability and validity studies; infringement analysis; and preparation of licensing, consulting, confidentiality, and research agreements

1988 - 1992: Pennie & Edmonds, Law Clerk, Biotechnology Group
Preparation and prosecution of U.S. patent applications in the biotechnology, chemical and pharmaceutical fields and interactions with foreign associates regarding foreign prosecution; assisted in patentability studies, validity studies, and infringement analyses and assisted in the preparation of consulting, confidentiality and licensing agreements

PRE-LEGAL EXPERIENCE:

1986 - 1988: Research Fellow, Sloan Kettering Institute
Investigated the mechanism of the block in splicing of influenza viral NS1 mRNA to NS2 mRNA <u>in vitro</u> using molecular biological and biochemical approaches

1979 - 1986: Predoctoral Fellow, Johns Hopkins University
Formulated methods for synthesizing the antisense nonionic oligonucleotide analogs, oligonucleoside methylphosphonates; studied the effects of oligonucleoside methylphosphonate sequences on the synthesis of VSV (vesicular stomatitis virus) proteins in cell culture and in vitro

1979: Undergraduate Research Associate, Argonne National Laboratory.
Analyzed bile acids isolated from the bile, urine, or serum from children with cholestatic liver disease using gas chromatography and gas chromatography/mass spectroscopy

HONORS, AWARDS, AND FELLOWSHIPS:

1988-1992: Richardson Scholar, Brooklyn Law School

1988-1990: Dean's List, Brooklyn Law School

1986-1988: American Cancer Society Postdoctoral Fellow,
Sloan Kettering Institute

1984: Student Research Award, Delta Omega Honorary
Public Health Society

1979-1986: Predoctoral Training Grants: Predoctoral trainee, NIH (1979-1982);
Albert Szent-Gyorgyi Foundation (1982-1986)

May 1979: Graduated with General Honors and Honors in Chemistry from Goucher College
Louise Kelly Award in Chemistry, Goucher College

1979: Undergraduate Research Program (January-May) and Summer Graduate Student Program (June-August) at Argonne National Laboratory, Argonne, Illinois

FACULTY APPOINTMENTS

Angel Financing:Navigating the Legal & Business Issues, Citybar Center for CLE, The Association of the Bar of the City of New York, November 28, 2000

Organizer and instructor at National Association of Patent Practitioner's 2000 Short Course on Nuts and Bolts of Patent Prosecution, July 2000

Instructor, Sixth, Eighth, Ninth and Tenth Annual Patent Prosecution Workshops: Advanced Claim Drafting and Amendment Writing (1996, 1998, 1999, 2000)

Law Seminars International: Biotechnology Key Legal & Business Issues, November 18-19, 1999, Seattle Washington

ADDITIONAL SKILLS

Computer literate, LEXIS, WESTLAW, DIALOG, Internet User

MEMBERSHIPS:

National Association of Patent Practitioners: Member, Board of Directors and Chairperson of Education Committee
American Intellectual Property Law Association
Eastern New York Intellectual Property Law Association
American Bar Association, Intellectual Property Section
Association of the Bar of the City of New York
Association for Women in Science
Association of University Transfer Managers
Westchester Women's Bar Association
International Intellectual Property Society

ORAL PRESENTATIONS

"Alternative Career Opportunities in Intellectual Property Property Law", New York Biotechnology Association, Women in Bioseciences Section Meeting, June 2000

"Why Deposit Biological Materials?" New York, New Jersey, Connecticut, and Pennsylvania Joint Seminar on Developments in Patent Law, April 2000

"Inventorship", National Association of Patent Practitioners meeting, July 1999
Panel chair, "Interactions Between In-House and Law Firm Patent Counsel to Develop Intellectual Property Strategy", BIO '98, June 1998

"What to Claim in Biotechnology Patent Applications", National Association of Patent Practitioners meeting, October 1997

"*In re Deuel,* Obviousness Standard for Biotechnology", BIO '96, June 1996

PUBLICATIONS:

Patents:

Have participated in the preparation and/or prosecution of over 150 patents. Representative patents are listed below:

U.S. Patent No. 6,060,305, "Non-toxic, non-toxigenic, non-pathogenic Fusarium expression system"

U.S. Patent No. 5,919,697, "Color Clarification Methods"

U.S. Patent No. 5,843,753, "Metalloprotease having increased activity"

U.S. Patent No. 5,770,371, "Modification of cryptic splice sites in heterologous genes expressed in fungi"

U.S. Patent No. 5,726,202, "Benign prostatic hypertrophy"

U.S. Patent No. 5,707,798, "Identification of ligands by selective amplification of cells transfected with receptors"

U.S. Patent No. 5,602,032, "Bacillus thuringiensis mutants which produce high yields of crystal delta-endotoxin"

U.S. Patent No. 5,580,560, "Modified factor VII/VIIa"

U.S. Patent No. 5,525,193, "Use of monocomponent cellulase for removing inks, coatings, and toners from printed paper"

U.S. Patent No. 5,354,760, "Crystalline Tiagabine monohydrate, its preparation and use"

Legal-related Publications:

Agris, C.H. (2000) "Biotechnology Applications: Depositing Biological Materials" Intellectual Property Today 7:12-13

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Agris, C.H. (1999) "Intellectual property protection for plants", Nature BioTechnology 17:197-198

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Agris, C.H. (1998) "International Patent Filing", Nature BioTechnology 16:479-480

Agris, C.H. (1996) "Prior Art Considerations When Patenting DNA Sequences", Nature Biotechnology 14:1309-1310

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Agris, C.H.; Nemeroff, M. E. and Krug, R. M. (1989) A block in mammalian splicing occurring after formation of large complexes containing U1, U2, U4, U5 and U6 small nuclear ribonucleoproteins, Mol Cell. Biol. 9:259-262

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Miller, P S; Agris, C.H.; Aurelian, L.; Blake, K.R.; Glave, S.A.; Lin, S-B; Murakami, A.; Reddy, M.P.; Smith, C.C.; Spitz, S.A.and Ts'o, P.O.P (1987), Matagen: (masking tape for gene expression): A family of sequence specific oligonucleoside methylphosphonates, Working group on: Molecular mechanisms of carcinogenic and antitumor activity, Vatican City, Italy, October 21-25, 1986, Pontif. Acad. Sci. Scr. Varia 70:169-204

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